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**REMARKS**

The present application was originally filed with 10 Claims. In a Restriction Requirement, the Examiner restricted the Claims into 6 Groups, as indicated below:

- I. Group I contains Claims 1-10, drawn in part to a subtilisin modified by an amino acid substitution at a position corresponding to position 27 in the sequence of subtilisin BPN';
- II. Group II contains Claims 1-10, drawn in part to a subtilisin modified by an amino acid substitution at a position corresponding to position 45 in the sequence of subtilisin BPN';
- III. Group III contains Claims 1-10, drawn in part to a subtilisin modified by an amino acid substitution at a position corresponding to position 170 in the sequence of subtilisin BPN';
- IV. Group IV contains Claims 1-10, drawn in part to a subtilisin modified by an amino acid substitution at a position corresponding to position 181 in the sequence of subtilisin BPN';
- V. Group V contains Claims 1-10, drawn in part to a subtilisin modified by an amino acid substitution at a position corresponding to position 251 in the sequence of subtilisin BPN'; and
- VI. Group VI contains Claims 1-10, drawn in part to a subtilisin modified by an amino acid substitution at a position corresponding to position 271 in the sequence of subtilisin BPN'.

The Examiner also made a species election requirement, as follows:

- A. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 1;
- B. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 14;
- C. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 49;
- D. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 61;

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- E. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 87;
- F. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 100;
- G. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 102;
- H. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 118;
- I. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 128;
- J. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 204; and
- K. A subtilisin variant comprising an additional amino acid substitution at the subtilisin BPN'-correspondent position 258.

In a Response filed December 23, 2005, Applicants elected the Claims in Group III (Claims 1-10, directed to substitution at position 170) without traverse. Applicants further elected the species set forth in Group E (position 87). Applicants respectfully requested rejoinder of the remaining species, upon determination that the elected species Claims are allowable.

Applicants appreciate the Examiner's entry of the Claim amendments. It appears that the formatting of the Response filed 25 September 2006 was inadvertently altered before filing such that the Claim amendments were not presented on a separate paper. Applicants also appreciate the Examiner's indication that the amendments filed in September 2006 overcome some of the rejections. Applicants also appreciate the Examiner's phone call to discuss the present application.

The Examiner has made the various rejections, addressed in the following order:

- 1) Claims 3, 5 and 7-10 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement;
- 2) Claims 3, 5 and 7-10 stand rejected, as allegedly not meeting the enablement requirement; and

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3) Claims 3, 5 and 7-10 stand rejected under 35 U.S.C. §103(a), as allegedly being obvious under *van der Osten et al.* (US Pat. No. 6,300,116), in view of *Hansen et al.* (US Pat. No. 6,605,458).

**1) The Written Description Requirement is Met**

The Examiner has rejected Claims 3, 5, and 7-10 under 35 U.S.C. §112, first paragraph as allegedly not meeting the written description requirement. While Applicants must respectfully disagree, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended the Claims to recite that the variant and precursor proteases are subtilisins. In addition, Applicants have added the recitation of specific amino acid substitutions as set forth in the Specification as filed. New Claim 13 also finds support in the Specification (See e.g., page 18, at line 4). Thus, no new matter is added in either the amendments or new Claim 13. Applicants reserve the right to pursue the cancelled and/or additional Claims in one or more subsequently filed applications. Applicants respectfully submit that the pending Claims are fully supported by the Specification and that the written description requirement is met. Applicants respectfully request that this rejection be withdrawn.

**2) The Enablement Requirement is Met**

The Examiner has rejected Claims 3, 5, and 7-10 under 35 U.S.C. §112, first paragraph, as allegedly not meeting the enablement requirement. Applicants note that the Examiner has admitted that the Specification is enabling for modifications of the members of the class of serine proteases known as subtilisins. As indicated above, while Applicants must respectfully disagree, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended the Claims to specifically recite that the Claims are directed toward subtilisin variants. Applicants respectfully submit that the pending Claims are fully enabled by the Specification and that the enablement requirement is met. Applicants respectfully request that this rejection be withdrawn.

**3) The Claims are Unobvious**

The Examiner has rejected Claims 3, 5 and 7-10 under 35 U.S.C. §103(a), as allegedly being obvious under *van der Osten et al.* (US Pat. No. 6,300,116), in view of *Hansen et al.* (US Pat. No. 6,605,458). In particular, the Examiner argues that Van der Osten teaches the R170

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substitution in combination with other substitutions such as P129K or F189K. However, as the Examiner admits Van der Osten do not teach the preparation of a subtilisin variant comprising any of the amino acid substitutions further to the R170S substitution as recited in the Claims (See, Office Action, page 5).

In regard to Hansen *et al.*, the Examiner argues that the R170S substitution may be combined in a variant with substitutions at positions 27, 36, 57, 76, 87, 97, 101, 104, 120, 123, 1676, 179, 206, 218, 222, 224, 235, and 274 (See, Office Action, page 5). However, Applicants respectfully submit that there may arguably be a suggestion of the combination of R170S with P129K or F189K. As neither the van der Osten *et al.* nor the Hansen *et al.* reference disclose the combination of substitutions in the amended Claims Applicants respectfully submit that the van der Osten *et al.* and Hansen *et al.* references do not render the Claims obvious. Applicants respectfully submit that the pending Claims are unobvious. Applicants reserve the right to pursue the cancelled and/or additional Claims in one or more subsequently filed applications. Thus, Applicants respectfully request that this rejection be withdrawn.

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**CONCLUSION**

As all of the grounds of the Examiner's rejections have been addressed and in view of the above remarks, the Applicants believe the pending Claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner has any questions regarding the present application he or she is encouraged to contact the undersigned.

Respectfully submitted,

Dated: June 11, 2007

  
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